REMARKS

Claims 1-7, 13, 14, 19 and 20 are pending in this application. Claims 8-12 and 15-18 have been previously cancelled because they were directed to non-elected subject matter.

REJECTION UNDER 35 U.S.C. § 102

Claims 1, 13, 14, 19 and 20 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Berk *et al.*, "Recombinant interleukin-1β inhibits elastin formation by a neonatal rat lung fibroblast subtype," J. OF BIOL. CHEM. (Feb. 15, 1991) 266: 3192-3197 ("the Berk article"). Claims 1, 13, 14, 19 and 20 also stand rejected under 35 U.S.C. § 102(b) as anticipated by Mauviel *et al.*, "Human recombinant interleukin-1β up-regulates elastin gene expression in dermal fibroblasts," J. OF BIOL. CHEM. (Mar. 25, 2993) 268(9): 6520-6524 ("the Mauviel article"). Finally, claims 1, 6, 13, 14, 19 and 20 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Archambault *et al.*, "Stretch and interleukin-1β induce matrix metalloproteinases in rabbit tendon cells *in vitro*," J. OF ORTHO. RES. (2002) 20: 36-39 ("the Archambault article").

Amended claim 1 recites a method for manipulating an intrinsic strain of a cell. The method comprises culturing the cell on a substrate or in a medium, thereby forming a cultured cell. A compound is administered to the cultured cells, either *in vivo* or *in vitro*, and resets the intrinsic strain of the cell. The intrinsic strain of the cell is reset by modulating a cytoskeletal gene. Claims 6, 13, 14, 19 and 20 ultimately depend from claim 1.

Cytoskeletal genes differ from extracellular matrix genes. (See Banes *et al.*, "Mechanoreception at the cellular level: the detection interpretation, and diversity of responses to mechanical signals," BIOCHEM. CELL BIOL. (Jul-Aug 1995) 73(7-8): 349-365 ("the Banes article"). The Banes article is attached to the IDS submitted with this Amendment) The cytoskeleton comprises biopolymers actin microfilaments, microtubules, and intermediate filaments. (Stamenović *et al.*, "Cellular responses to mechanical stress invited review: engineering approaches to cytoskeletal mechanics," J. APPL. PHYSIOL. (2000) 89: 2085-2090 ("the Stamenović article"); Qi *et al.* "IL-1β decreases the elastic modulus of human tenocytes," J. APPL. PHYSIOL. (Apr 20, 2006) 101: 189-195, 189 ("the Qi Cytoskeleton article"). The

Stamenović article is attached to the IDS submitted with this Amendment. The Qi Cytoskeleton article is attached to this Amendment as Exhibit A) In contrast, the extracellular matrix is composed mainly of elastin and collagen. (Qi *et al.*, "Interleukin-1β increases elasticity of human bioartificial tendons," TISSUE ENGINEERING (Nov. 10, 2006) 12: 2913-2925, 2913 ("the Qi Extracellular Matrix article"); Farahani *et al.*, "The hypothesis of 'biophysical matrix contraction': wound contraction revisited," INT'L WOUND JOURNAL (2008) 5: 477-482 ("the Farahani article"). The Qi Extracellular Matrix article and the Farahani article are attached hereto as Exhibits B and C, respectively.) Thus, modulating the extracellular matrix does not necessarily mean the cytoskeleton will be modulated because different proteins are involved and the proteins are positioned in different locations (i.e. inside the cell versus outside the cell).

In summary, the claimed invention is directed to modulating the cytoskeleton of a cell, whereas the cited references are directed to modulating the extracellular matrix. Thus, the cited references teach altering the expression or amount of proteins such as elastin that are positioned outside of a cell. In contrast, the claimed invention is directed to modulating the expression or amount of proteins located inside the cell, such as actin.

Specifically, the Berk article discloses data that recombination IL-1β decreases steady state levels of elastin mRNA and elastin accumulation, and can selectively regulate the accumulation of elastin and collagen. (The Berk article at abstract.) Elastin and collagen are proteins present in the extracellular matrix. (The Qi Extracellular Matrix article at 2913.) Since the claimed invention is directed to modulating intrinsic strain of a cell (i.e. the intracellular cytoskeleton) (e.g. actin), and the Berk article discloses modulating the extracellular matrix (e.g. collagen), the Berk article does not teach or suggest each and every element recited in claim 1, or any claim that depends from claim 1.

The Mauviel article discloses that IL-1β effects elastin gene expression in human skin fibroblasts. As discussed above, elastin is an extracellular matrix protein. (The Qi Extracellular Matrix article at 2913.) Since the claimed invention is directed to modulating intrinsic strain of a cell, and the Mauviel article discloses modulating the extracellular matrix, the Mauviel article does not teach or suggest each and every element recited in claim 1, or any claim

that depends from claim 1.

The Archambault article teaches that IL-1β increases the expression and production of matrix metalloproteinases ("MMPs"). MMPs degrade extracellular proteins, such as elastin and collagen. (The Qi Extracellular Matrix article at page 2914.) In contrast, the claimed invention is directed to a method of manipulating an intrinsic strain (i.e. intracellular cytoskeleton) of a cell, not the extracellular matrix or, more particularly, enzymes that degrade the extracellular matrix. Since Archambault is directed to degrading the extracellular matrix, it does not teach or suggest each and every limitation recited in claim 1, or any claim that depends from claim 1.

For these reasons, Applicants respectfully request that these rejections be reconsidered and withdrawn.

REJECTION UNDER 35 U.S.C. § 103

Claims 1-7, 13, 14, 19 and 20 stand rejected under 35 U.S.C. § 103(a) as being obvious over the Archambault article in view of U.S. Patent No. 6,472,202 to Banes ("the '202 Patent"). As discussed above, the Archambault article teaches degrading the extracellular matrix of a cell rather than the cytoskeleton. This deficiency is not overcome by the '202 Patent, which is directed to applying mechanical strain to a cell. (The '202 Patent at abstract.) Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

DOUBLE PATENTING REJECTION

Claims 1-5, 13, 14, 19 and 20 have been provisionally rejected on the ground of non-statutory obviousness-type double patenting as being obvious over claims 2, 3, 27, 28, 30 and 31 in co-pending United States Patent Application No. 11/076,425 ("the '425 Application"). The '425 Application is now abandoned because a response was not filed to the Office Action dated August 18, 2009. In view of this abandonment, withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the amendments to the claims and remarks, Applicants respectfully request that the rejections asserted against the claims be reconsidered and withdrawn, and that claims 1-7, 13, 14, 19 and 20 be allowed.

Respectfully submitted,

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